

Gebauer's Pain Ease®

Topical Anesthetic Skin Refrigerant

TECHNICAL DATA DOCUMENT



*Gebauer's
Pain Ease®*

 **Gebauer Company**

GEBAUER'S PAIN EASE®

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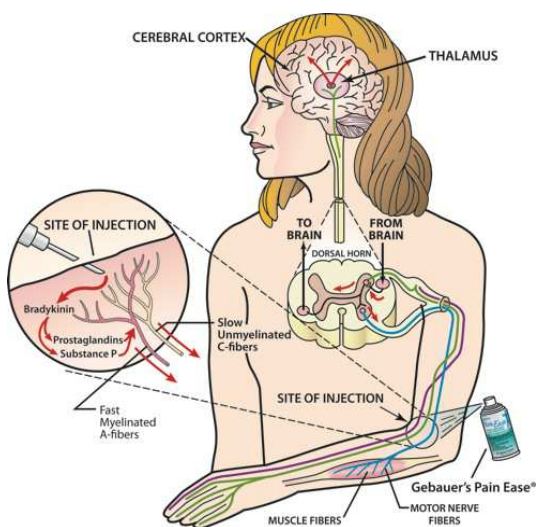
Description

Gebauer's Pain Ease consists of a proprietary blend of 1,1,1,3,3-Pentafluoropropane (HFC-245fa) and 1,1,1,2-Tetrafluoroethane (HFC-134a) that produces an instantaneous cooling effect upon contact with the skin, intact mucous membranes and minor open wounds. The product is delivered in the form of an aerosol in either a mist or medium stream spray. Upon contact with the skin or mucosal membranes, the product evaporates immediately. The evaporation of the product, once it makes contact with the skin, is due to the low evaporation rate created by the chemical blend and the unique delivery system.

Gebauer's Pain Ease is non-flammable and non-ozone depleting.

Mechanism of Action

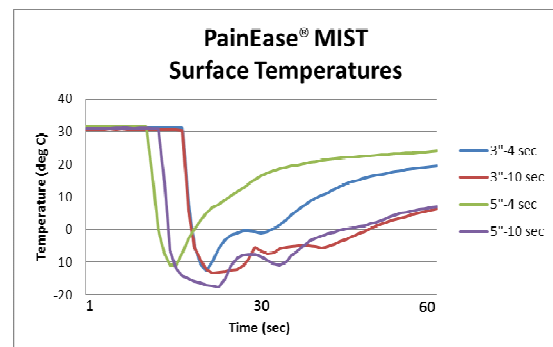
Gebauer's Pain Ease can be topically applied to intact skin, intact oral mucous membranes and minor open wounds. It creates an instantaneous cooling effect on the surface of the application site by the immediate evaporation of the product from the skin surface. The coldness created by the spray decreases the nerve conduction velocity of the C fibers and A-delta fibers that make up the peripheral nervous system, thus interrupting the nociceptive inputs to the spinal cord (Lehmann and Delateur 1990).



Cooling Effect: When Gebauer's Pain Ease begins to evaporate from the surface of the target area after application, a cooling effect results. The cooling sensation produced is directly related to the type of stream and the distance from the point of contact.

The mist produces very fine droplets that create instantaneous cold at the points of contact. The fine droplets are dispersed in a circular pattern with an approximate two inch diameter when sprayed from a distance of four inches from the target. The medium stream spray produces a pinpoint stream that contacts the skin surface at a specific single location.

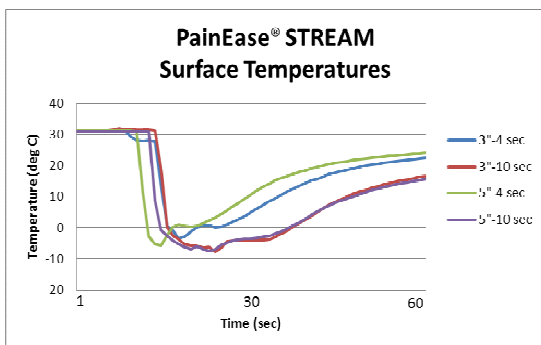
As the distance from the target surface is increased, the dispersion of the droplets in both the mist and medium stream is increased. Increasing the surface area of contact and decreasing the size of the droplets increases the evaporation rate. The increase in evaporation rate correlates to an increase in the cooling effect.



* Data generated in support of Merrick MA, Martin KM, (2012, May).

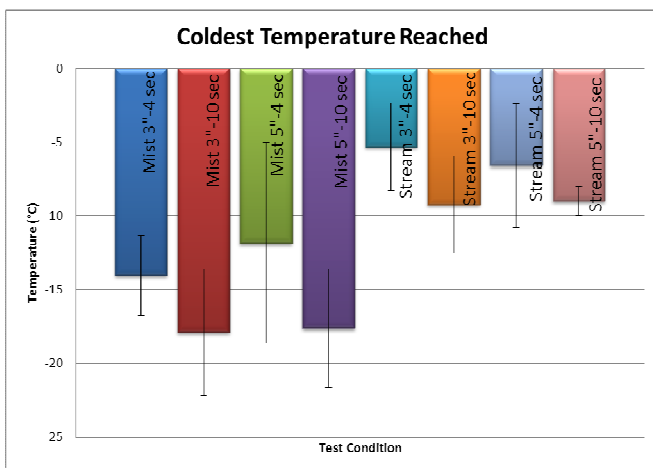
Gebauer's Pain Ease Mist is most effective for general cooling of the skin, intact mucous membranes and minor open wounds where precise contact is not indicated. Since the evaporation rate is increased, a more intense cooling effect will be created at the initial point of application over a larger area.

GEBAUER'S PAIN EASE® Topical Anesthetic Skin Refrigerant



* Data generated in support of Merrick MA, Martin KM, (2012, May).

Gebauer's Pain Ease Medium Stream is most effective for creating an anesthetic effect on the skin or intact mucous membranes at a specific pinpoint site.



* Data generated in support of Merrick MA, Martin KM, (2012, May).

According to a study performed at The Ohio State University by Dr. M. Merrick, the comparison between Gebauer's Pain Ease Mist and Stream products yielded results that indicated the lowest average temperature reached over various distances and dispensing times. The data of the clinical trial concluded that on average the mist product showed a lower temperature reached on the skin compared to the stream product. However both Gebauer Pain Ease product variations demonstrated an initial

cooling that created an anesthetic effect on the skin. (Merrick and Martin 2012)

Indications and Use

Gebauer's Pain Ease medium stream and the mist configurations are safe for use on skin, intact mucous membranes (oral cavity, nasal passages and lips) and minor open wounds for the following indications:

Pain Management due to:

- Injections such as venipuncture, IV starts and cosmetic procedures.
- Minor surgical procedures such as lancing boils, incisions, drainage of small abscesses and suturing.
- Minor sports injuries such as sprains, bruising, cuts and abrasions.

The medium stream is also intended as a counterirritant in the management of:

- Myofascial Pain
- Restricted Motion
- Muscle Tension

Contraindications

Gebauer's Pain Ease is contraindicated in individuals with a history of hypersensitivity to HFC-245fa and HFC-134a. If skin irritation develops, discontinue use.

Warnings

Gebauer's Pain Ease is for external use, for use on minor wounds and for use on intact mucous membranes only.

The contents are under pressure. Do not puncture or incinerate the container. Do not expose to heat or store at temperatures above 50°C (120°F). Dispose of in accordance with local and national regulations.

GEBAUER'S PAIN EASE®

Topical Anesthetic Skin Refrigerant

Adverse Reactions

Freezing of the skin can occasionally alter the skin pigmentation. Injury to the skin due to extreme cold or irritation may create post-inflammatory hypopigmentation due to death of melanocytes in the epidermal layer of the skin. This reaction may be more apparent in people with dark complexions (Taylor 1997).

It often takes several months for the skin pigment to return to its unaltered state. The effects of post-inflammatory hypopigmentation may be permanent (Goodheart 1999).

Precautions

The following precautions should be observed when using Gebauer's Pain Ease:

- 1) Do not spray in the eyes.
- 2) Do not use this product on persons with poor circulation or insensitive skin.
- 3) When used to produce local freezing of tissues, adjacent skin areas should be protected by an application of petroleum.
- 4) The freezing and thawing process may be painful, and freezing may lower local resistance to infection and delay healing.
- 5) Over application of the product might cause frostbite and/or alter skin pigmentation.
- 6) Do not use on large areas of damaged skin, puncture wounds, animal bites or serious wounds.
- 7) Apply only to intact mucous membranes.
- 8) Do not use on genital mucous membranes.

Biocompatibility

All biocompatibility and toxicology testing was performed in accordance with ISO 10993 Guidelines and the FDA's Blue Book Memorandum G-95. All testing was performed by independent testing laboratories.

Cardiac Sensitization: HFC-245fa and HFC-134a are known to be cardiac sensitizers when inhaled in quantities greater than 80,000 ppm (Rusch, Combs, and Hardy 1995) and 44,000 ppm (Talmage, Rusch, Benson, and Stoll 1998) respectively. In studies performed on beagle dogs, fatal ventricular fibrillation was seen at 74,000 ppm, one incident of ventricular defibrillation occurred at 44,000 ppm, and no incidents of cardiac sensitization were seen at 34,100 ppm for HFC-245fa (Rusch, Combs, and Hardy 1995).

Cytotoxicology: Gebauer's Pain Ease was tested for cytotoxicity in accordance to ISO 10995-5, *Tests for Cytotoxicity – In Vitro Tests* and was found to be non-toxic when used as recommended. Acute cytotoxicity of the product was tested by observing the % inhibition of the cell viability of human keratinocyte HaCat cells when Gebauer's Pain Ease was "sprayed" on the cells for both 5 seconds and 15 seconds and incubated at 5% CO₂ and 37°C. Neither the 5 second nor the 15 second dosage was found to be cytotoxic and had little effect on the HaCat cell viability.

Dermal Sensitization: A dermal sensitization study was performed in accordance with ISO 10993-10, *Tests for Irritation and Sensitization* on guinea pigs using a modified Buehler method to determine the dermal sensitization in the guinea pig with repeated dermal exposure of Gebauer's Pain Ease. The animals were exposed to the product three times a week for three weeks. The animals remained in good health throughout the induction phases and no abnormal clinical findings were observed. There was slight erythema noted in one animal at the first induction exposure. There were no incidents of edema noted during the induction phases. During the challenge phase of the study, one animal had minimal erythema at the 24 hour stage. No incidents of edema were observed during the challenge stage. Based on these results, Gebauer's Pain Ease did not produce dermal sensitization in guinea pigs under the conditions of the study.

Acute Dermal Toxicity: An acute dermal toxicity study was performed in accordance to ISO 10993-

GEBAUER'S PAIN EASE®

Topical Anesthetic Skin Refrigerant

11, *Tests for Systemic Toxicity* on Sprague-Dawley Rats to determine the acute dermal toxicity of Gebauer's Pain Ease. No animals died during the study and the animals gained weight as expected. Observations made at 1 hour, 2.5 hours, 4 hours, 1 day and daily up to 14 days showed no clinical effects as a result of the treatment. Necropsy of the tissues at the end of the study were found to be grossly normal. Gebauer's Pain Ease does not produce acute dermal toxicity.

Oral Irritation: A study was executed in accordance to ISO 10993-10, *Tests for Irritation and Sensitization* on Syrian Hamsters to determine the acute oral irritation produced by exposure to Gebauer's Pain Ease. A group of hamsters was exposed to the product by directly spraying the cheek pouch with product on a single occasion and observing for signs of irritation. In addition, a second group of hamsters was exposed to the product five times in a four hour period by directly spraying the cheek pouch with product and observing for signs of irritation. Oral observations showed that no irritation was observed for the single dosage group, and an irritation score of <1 was observed for the 5 doses over a 4 hour period, which shows that the irritation observed was between no erythema and very slight erythema (hardly perceptible). Histopathology was performed on the cheek pouches and compared to the control group. Based on the results of the oral irritation histopathology report, Gebauer's Pain Ease is a non-irritant when applied as a single dose. Gebauer's Pain Ease is a minimal irritant when applied five times over a period of four hours.

The results of this study confirm the indication for use of Gebauer's Pain Ease on intact mucous membranes.

Inhalation Toxicity: Gebauer's Pain Ease has a very low to minimal toxicity by inhalation. Studies performed on mice/rats showed that HFC-245fa and HFC-134a were non-toxic by inhalation. A series of 28-Day and 13 week Inhalation studies were performed using HFC-245fa. In a snout-only exposure to HFC-245fa with mice, no lethality was

seen even with exposure levels over 100,000 ppm for 4 hours. In rats, 4 hour whole body exposures to levels as high as 203,000 ppm did not cause mortality. Although some signs of mild central nervous system depression were seen with exposures at 143,000ppm and 203,000 ppm, these were only seen during exposure, with the animals showing recovery within 30 minutes of the end of the exposure period. These findings indicate that HFC-245fa is not acutely toxic by inhalation and that even high level exposures do not result in marked signs of toxicity (Rusch, Coombs, and Hardy 1995).

Subchronic and chronic studies were carried out in the rat with exposures to HFC-134a by inhalation. Repeated exposure to 50,000 ppm of HFC-134a for 13, 52, and 104 weeks elicited no effect on clinical condition, growth, and survival, or on a variety of hematological, clinical chemistry, and urinary parameters. Treatment-related pathological changes were seen only at study termination at 2 years and were confined to increased incidence of Leydig cell hyperplasia and adenoma in male rats exposed to 50,000 ppm. The tumors were benign and not life threatening. These studies demonstrate that HFC-134a has very low toxicity by inhalation (Collins, Rusch, Sato, Hext, and Millishcher 1995).

Effects on Fertility: Gebauer's Pain Ease is safe for use during pregnancy when used as directed. Studies performed on rats showed that HFC-245fa and HFC-134a were non teratogenic and did not cause fetal effects at levels of 50,000 ppm. Rats exposed daily to levels of 50,000 ppm HFC-134a for six hours from day 6 to day 19 of gestation at the 50,000 ppm level had a reduction in body weight and food consumption. No significant effects were seen on fetal parameters. Pup weight, litter size, and uterine weights were slightly reduced when compared to controls. The incidents of malformation, skeletal and visceral anomalies and skeletal variants was comparable to the control group (Rusch, Coombs, and Hardy 1995). When exposed daily to 300,000 ppm of HFC-134a during day 6 through 15 of gestation, there was a significant reduction in fetal weight and increase in

GEBAUER'S PAIN EASE®

Topical Anesthetic Skin Refrigerant

skeletal variations (Collins, Rusch, Sato, Hext, and Millischer 1995).

Carcinogenesis: Gebauer's Pain Ease is not carcinogenic. When HFC-134a was administered to rats for 104 weeks, there was a slight increase in the incidence of testicular Leydig cell adenomas in the male rats. This type of tumor does not progress to malignancy in humans, and the lack of genotoxicity support the conclusion that HFC-134a is not carcinogenic (Collins, Rusch, Sato, Hext, and Millischer 1995). Genotoxicity in HFC-245fa has not been shown and various inhalation studies have produced no carcinogenic effects (Rusch, Coombs, and Hardy 1995).

Performance

The Gebauer Company has executed the following performance testing to verify that Gebauer's Pain Ease provides a safe and effective product.

Number of Applications: Gebauer's Pain Ease products have approximately 50 doses per can when applied for an average time of 5 seconds per dose.

Chemical Compatibility: Chemical compatibility testing was performed by the manufacturers of HFC-245fa and HFC-134a to determine the chemical stability of the Gebauer's Pain Ease blend. In chemical stability studies, both HFC-245fa and HFC-134a were found to be stable at temperatures up to 400°F. A mixture of HFC-245fa and HFC-134a was stored in a tin-plated aerosol can with a valve and dip tube for a period of two months in ambient conditions. Results from GC/MS analysis confirmed that there were no new compounds formed during the storage due to chemical incompatibility.

Material Compatibility: Material compatibility data for the following materials has been performed with Gebauer's Pain Ease in order to show package integrity. Results of the compatibility analysis can be found in Table 1.

The packaging materials tested show excellent material compatibility characteristics. Based on the results, there was no evidence of leachables or breakdown of the packaging components that would lead to contamination or product malfunctioning.

Table 1
Material Compatibility of
Gebauer's Pain Ease

Material	Compatibility
Butyl	Excellent
Poly-propylene	Excellent
Nylon	Excellent
Epoxy	Excellent
Buna N	Excellent

Product Stability: Stability studies are routinely conducted to determine the chemical stability and packaging integrity of Gebauer's Pain Ease in accordance with Q1A Stability Testing of New Drug Substances and Products, ICH Guidance for Industry; Rev. 1, August 2001. Stability is performed over the shelf-life of the product. This testing consists of the following: appearance, percent purity, and ratio composition. Table 2 contains the results of the stability study.

Table 2
Results of Stability Testing for Gebauer's Pain Ease

	Appearance	Ratio Composition	% Purity
Initial	N/A	Pass	99.9
1 Year	No change observed	Pass	99.9
2 Year	No change observed	Pass	99.9

Based on the results of the stability testing, Gebauer's Pain Ease is determined to be chemically stable over the two year shelf-life.

GEBAUER'S PAIN EASE®

Topical Anesthetic Skin Refrigerant

Microbiological Testing

Controlled Manufacturing Environment: The chemicals themselves that are used to comprise Pain Ease are filtered to screen out particulates larger than 0.2 microns. In addition, Pain Ease is filled in a controlled environment that is monitored for temperature, humidity and positive pressure. The air in this manufacturing environment has HEPA filtration which maintains air particulates to levels established for a Class 100,000 clean room.

The room also undergoes microbial monitoring during each manufacturing run of Pain Ease. It includes an assessment of the air, surfaces, as well as the personnel. This assessment is based on the recommendations specified in the United States Pharmacopeia (USP) General Chapter <1116>, *Microbial Evaluations of Cleanrooms and Other Controlled Environments*.

Microbial Examination: Once the product has been manufactured, each lot of Pain Ease is tested to USP <61> and USP <62> by an outside, independent laboratory. Lots are not released until the testing is completed and all microbiological results meet acceptance criteria.

USP <61>, *Microbial Examination of Nonsterile Products: Microbial Enumeration Tests* is performed to determine the total aerobic microbial count (TAMC) and total yeast and mold counts (TYMC) present.

USP <62>, *Microbial Examination of Nonsterile Products: Tests for Specified Microorganisms* is performed to test the presence/absence of *Staphylococcus aureus* and *Pseudomonas aeruginosa*.

Flammability

Gebauer's Pain Ease is non-flammable. It can be used in conjunction with ultrasound, x-ray, laser and cautery equipment. When using cautery equipment, special care should be taken to determine that the product has completely

evaporated from the surface of contact to prevent possible decomposition due to extreme heat. When product is directly exposed to sources of high temperatures, toxic or corrosive decomposition may occur producing halogens, halogen acids and possibly carbonyl halides.

Dosage and Administration

To apply Gebauer's Pain Ease from the aerosol can, hold the can upright over the treatment area approximately 8 to 18 cm (3 to 7 inches) away from the application site. Press the actuator button firmly, allowing Pain Ease to spray from the can.

If the aerosol can quits spraying, turn the white actuator button approximately ½ turn, then point the nozzle at the treatment area and press the actuator button firmly.

Pre-Injection Anesthesia:

Prepare the syringe. Swab the treatment area with an antiseptic. Spray the treatment area with Pain Ease continuously for 4 to 10 seconds from a distance of 8 to 18 cm (3 to 7 inches) until the skin just turns white. Do not frost the skin/area. Avoid spraying the target area beyond this state. With the skin taut, quickly introduce the needle. Reapply as needed. Follow these directions for other types of needle insertion procedures such as starting IV's and venipuncture.

Topical Anesthesia in Minor Surgery:

Clean the operative site with a suitable antiseptic. Apply petroleum to protect the adjacent area. Spray Pain Ease on the treatment area continuously for 4 to 10 seconds from a distance of 8 to 18 cm (3 to 7 inches) until the skin just turns white. Do not frost the skin/area. Avoid spraying the target area beyond this state and promptly make incision. The anesthetic action of Pain Ease lasts a few seconds to a minute. Reapply as needed.

Temporary Relief of Minor Sports Injuries:

The pain of bruises, contusions, swelling, minor sprains, cuts and abrasions may be controlled with

GEBAUER'S PAIN EASE®

Topical Anesthetic Skin Refrigerant

Pain Ease. The amount of cooling depends on the dosage. Dosage varies with duration of application. The smallest dose needed to produce the desired effect should be used. The anesthetic effect of Pain Ease rarely lasts more than a few seconds to a minute. This time interval is usually sufficient to help reduce or relieve the initial trauma of the injury. Spray Pain Ease on the target area continuously for 4 to 10 seconds from a distance of 8 to 18 cm (3 to 7 inches) until the skin just turns white. Do not frost the skin/area. Avoid spraying the skin beyond this state. Reapply as needed.

Spray and Stretch technique for Myofascial Pain (Pain Ease Medium Stream Spray only):

Pain Ease Medium Stream Spray may be used as a counterirritant in the management of myofascial pain, restricted motion and muscle tension. Clinical conditions that may respond to Pain Ease Medium Stream Spray included low back pain (due to tight muscles), acute stiff neck, torticollis, acute bursitis of the shoulder, tight hamstrings, sprained ankle, tight masseter muscles and referred pains due to irritated trigger points. Relief of pain facilitates early mobilization and restoration of muscle function. The Spray and Stretch Technique is a system that involves three stages: Evaluation, Spraying and Stretching. The therapeutic value of the Spray and Stretch Technique is most effective when the practitioner has mastered all of the stages and applies them in the proper sequence.

- 1) **Evaluation:** If the patient has been evaluated to have muscle tension and restricted motion caused by an active, irritated trigger point, then proceed to Step 2.
- 2) **Spraying:**
 - A. Have the patient assume a comfortable position.
 - B. Take precautions to cover the patient's eyes if spraying near the face.
 - C. Hold the can upright. From a distance of 30 to 46 cm (12 to 18 inches), aim the stream so that it meets the skin at an

acute angle lessening the shock of impact.

Direct the spray in parallel sweeps 1.5 to 2 cm (0.5 to 1 inch) apart at the rate of approximately 10 cm per second (4 inches per second). Continue until the entire muscle has been covered. The number of sweeps is determined by the size of the muscle. The spray should be applied from the muscle attachment over the trigger point, through and over the reference zone.

- 3) **Stretching:** Passively stretch the muscle during spray application. Gradually increase the force with successive sweeps. As the muscle relaxes, smoothly take up the slack by establishing a new stretch length. It is necessary to reach the full normal length of the muscle to completely inactivate the trigger point and relieve the pain. Rewarm the muscle. If necessary, repeat the procedure. Apply moist heat for 10 to 15 minutes following treatment. For lasting benefit, eliminate any factors that perpetuate the trigger mechanism.

GEBAUER'S PAIN EASE®

Topical Anesthetic Skin Refrigerant

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Ordering Information

Gebauer's Pain Ease is available in the following configurations:

Gebauer's Pain Ease Medium Stream
U.S. Order No. 0386-0008-03
Intl. Order No. 0386-0008-25
3.5 fl. Oz. (103.5 mL) Aerosol Can

Gebauer's Pain Ease Mist Spray
U.S. Order No. 0386-0008-02
Intl. Order No. 0386-0008-45
3.5 fl. Oz. (103.5 mL) Aerosol Can
Revision 01/07

Rx only: The FDA has designated Gebauer's Pain Ease Mist Spray and Medium Spray as Prescription only (Rx) medical devices. This designation means that Pain Ease can be sold to and purchased by any healthcare practitioner who is licensed by the state in which they practice. Healthcare practitioners include doctors, chiropractors, physical therapists, nurses, etc. Any healthcare professional should be able to purchase prescription devices without restriction.

Gebauer's Pain Ease may be purchased by any patient who receives a prescription or "other order" which is defined as an instruction from a healthcare practitioner to use a prescription device.